Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Successful treatment of tocilizumab and ivermectin for a patient with ARDS due to COVID-19

Dear Editor:

Acute respiratory distress syndrome (ARDS) is one of the consequences of the cytokine release syndrome (CRS) triggered by coronavirus disease 2019 (COVID-19).[1] Tocilizumab (TCZ), a recombinant IL-6 inhibitor, is a potentially beneficial treatment for CRS caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.[2] Ivermectin, an antiparasitic drug, acts as a potential inhibitor of the coronavirus.[3] The combination of TCZ and Ivermectin could be a potential treatment for COVID-19-related ARDS.

A 68-y/o female was admitted to the hospital for COVID-19 after returning from Indonesia. The chest radiograph revealed bilateral subpleural infiltrates (Fig. 1A). She was tested positive for SARS-CoV-2 and treated with hydroxychloroquine and azithromycin on hospital day 2. ARDS (Fig. 1B) had developed on hospital day 4/ICU day 1, and intubation with lung protective-strategy and prone positioning was performed due to PaO_2/FiO_2 ratio at 60 mmHg. Both hydroxychloroquine and azithromycin were discontinued due to QTc prolongation (709 ms) on hospital day 9/ICU day 6. We prescribed single dose of TCZ 240 mg for ARDS and checked for hyper-inflammatory response, including C-reactive protein (CRP) at 30.42 mg/dL (reference range: 0—0.5 mg/dL), lactate dehydrogenase (LDH) at 667 U/L (reference range: 125—220 U/L) and ferritin at 4125.77 ng/mL (reference range: 4.63—204 ng/mL) on hospital day 10/ICU day 7. Single dose of Ivermectin 12 mg was given on hospital day 12/ICU day 9 due to positive result of SARS-CoV-2 in sputum collected on hospital day 10/ICU day 7. After the Ivermectin treatment, the patient had 3 negative results on consecutive sputum examinations during hospital days 15—17/ICU days 12—14, and the PaO_2/FiO_2 ratio increased gradually (from 91, 154 to 230 mmHg). Her chest radiograph (Fig. 1C) showed improvement and hyper-inflammatory markers decreased gradually (CRP from 30.42 to 0.48 mg/dL, LDH from 667 to 342 IU, and ferritin from 4125.77 to 1000 ng/mL), which all confirmed our suspicion that the CRS induced by SARS-CoV-2 was the cause of ARDS. She had a smooth hospital discharge, but living with subpleural fibrosis (Fig. 1D).

During the initial stage of infection, SARS-CoV-2 could trigger an adaptive immune response to fight against virus in our body and lead to a phase of CRS that cause ARDS.[1] Previous reports demonstrated that, in addition to CRP, LDH and ferritin, the IL-6 levels were elevated during SARS-CoV-2 infection.[2] CRP, LDH and ferritin could be used to predict the acuteness, severity and prognosis of COVID-19, and considered as a surrogate marker for IL-6 level.[2,4] The hypothesized mechanism of Ivermectin was implicated in the blockade of viral protein transport in the nucleus of target cell, and significantly reducing the coronaviral RNA by more than 90% in 24 h. However, the report of clinical trials on Ivermectin for the treatment of COVID-19 are not yet available.[3] In this case, Ivermectin was the only one choice that could possibly treat SARS-CoV-2 in our patient under the circumstances of limited availability of Lopinavir/Ritonavir and Remdesivir, as well as the adverse effects in hydroxychloroquine and azithromycin.[5] The rationale of combination with Ivermectin and TCZ is to stop the coronavirus and to deal with the CRS-induced ARDS. To our knowledge, this is the first and unique reported case of successful treatment in the combination of TCZ and Ivermectin for ARDS induced by COVID-19. The combination therapy of IL-6 inhibitor and potential anti-coronavirus agent deserves further investigation in SARS-CoV-2 related ARDS.

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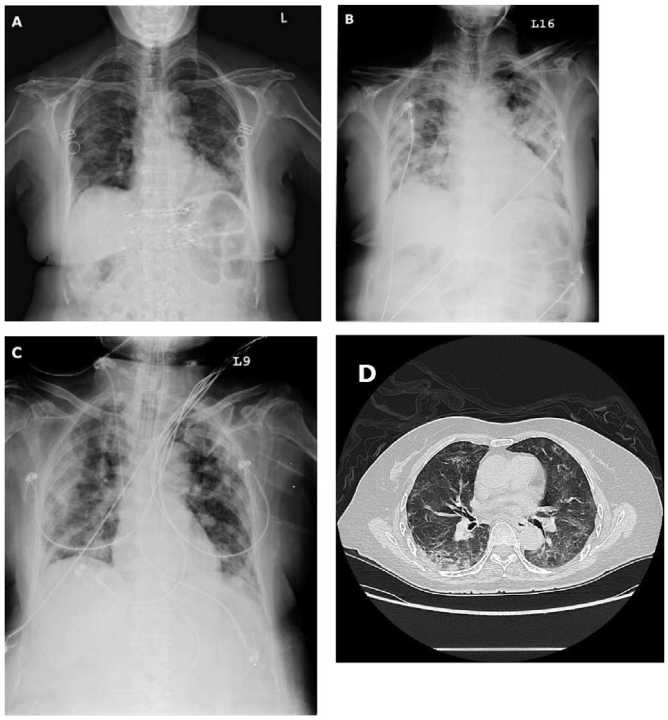

Figure 1. Serial chest radiographs revealed changes from bilateral subpleural infiltration (A) to bilateral subpleural patch of consolidation with ARDS (B), then turned to bilateral subpleural nodular infiltration (C), and chest CT scan showed subpleural fibrosis (D).

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